

CLAIMS

1. Process for the crosslinking of at least one polymer selected from polysaccharides and derivatives thereof, which is carried out in an aqueous solvent by the action of an effective and non-excessive amount of at least one crosslinking agent, characterized in that it is carried out on a mixture containing at least one low-molecular weight polymer and at least one high-molecular weight polymer.
- 5 2. Process according to claim 1, characterized in that said mixture contains a single polymer with at least two different molecular weights, at least one being low and at least one being high, and advantageously with two different molecular weights, one low and one high.
- 10 3. Process according to claim 1 or 2, characterized in that said polymer is a hyaluronic acid salt.
- 15 4. Process according to claim 3, characterized in that said hyaluronic acid salt is selected from the sodium salt, the potassium salt and mixtures thereof, and advantageously consists of the sodium salt.
5. Process according to any one of claims 1 to 4, characterized in that said mixture contains:
 - 20 - at least one hyaluronic acid salt of low molecular weight m , where $m \leq 9.9 \cdot 10^5$ Da, advantageously $10^4 \text{ Da} \leq m \leq 9.9 \cdot 10^5$ Da; and
 - at least one hyaluronic acid salt of high molecular weight M , where $M \geq 10^6$ Da, advantageously $10^6 \text{ Da} \leq M \leq 10^8$ Da, and very advantageously $1.1 \cdot 10^6 \text{ Da} \leq M \leq 5.10^6$ Da,
- 25 6. said low-molecular weight and high-molecular weight salts advantageously being of the same nature and very advantageously consisting of sodium hyaluronate.
6. Process according to claim 5, characterized in that said mixture has an intrinsic viscosity of less than 1900 ml/g.
- 30 7. Process according to claim 5 or 6, characterized in that said mixture contains more than 50% by weight, advantageously more than 70% by weight, of at least one hyaluronic acid salt of low molecular weight m , and less than 50% by weight, advantageously less than 30% by weight, of at least one hyaluronic acid salt of high molecular weight M .
- 35 8. Process according to any one of claims 5 to 7, characterized in that

said mixture contains at least 5% by weight of at least one high-molecular weight hyaluronic acid salt.

9. Process according to any one of claims 5 to 8, characterized in that said mixture contains about 90% by weight of the sodium salt of hyaluronic acid having a molecular weight of about 3.10^5 Da, and about 10% by weight of the sodium salt of hyaluronic acid having a molecular weight of about 3.10^6 Da.
10. Process according to any one of claims 1 to 9, characterized in that said crosslinking agent is selected from bifunctional crosslinking agents and mixtures thereof, is advantageously selected from epichlorohydrin, divinyl sulfone, 1,4-bis(2,3-epoxypropoxy)butane, 1,2-bis(2,3-epoxypropoxy) ethylene, 1-(2,3-epoxypropyl)-2,3-epoxycyclohexane, aldehydes such as formaldehyde, glutaraldehyde and crotonaldehyde, and mixtures thereof, and very advantageously consists of 1,4-bis(2,3-epoxypropoxy)butane.
11. Process according to any one of claims 1 to 10, characterized in that said effective and non-excessive amount of at least one crosslinking agent is such that the degree of crosslinking, defined by the ratio: $100 \times (\text{total number of reactive groups in said crosslinking agent}) / (\text{total number of disaccharide units in the polymer molecules present})$, is theoretically between 0.5 and 70%, advantageously between 4 and 50%.
12. Process for the preparation of an injectable monophase hydrogel of at least one crosslinked polymer selected from polysaccharides and derivatives thereof, characterized in that it comprises:
 - the crosslinking of a mixture according to any one of claims 1 to 11; and
 - the formulation of said crosslinked mixture, neutralized if necessary, into a solution buffered to a pH of between 6.5 and 7.5, advantageously of between 7 and 7.4 and very advantageously of between 7.1 and 7.3.
13. Process according to claim 12, characterized in that it comprises:
 - the crosslinking of a mixture according to any one of claims 3 to 11; and
 - the formulation of said crosslinked mixture, neutralized, into a solution buffered to a pH of between 7.1 and 7.3, at a concentration of between 10 and 40 mg/g, advantageously of between 20 and 30 mg/g.

14. Crosslinked polymer obtainable after a crosslinking process according to any one of claims 1 to 11 has been carried out.
15. Injectable monophase hydrogel obtainable after a preparative process according to claim 12 or 13 has been carried out.
- 5 16. Injectable monophase hydrogel according to claim 15, containing low-molecular weight sodium hyaluronate and high-molecular weight sodium hyaluronate in crosslinked form.